Effects of Systematically Administered Polyamines on Imipramine Immobility Action in Rats

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The main natural polyamines (PA)—spermidine (SPD) and spermine (SPM)—and their precursor putrescine (PUT) are organic cations of low molecular weight, ubiquitously distributed in living organisms. They are present in high concentration in the adult mammalian nervous system with wide regional variations.[1] Several and different experimental results suggest that natural PA may function as modulators of different central neurotransmitter systems, but little information concerning the possible pharmacological activity of PA or their interaction with drugs is available at present.[2,3] However, recent studies of particular significance to pharmacologists report on aminoglycoside antibiotic neomycin[4] and neuroprotective agent ifenprodil[5] interactions at a PA site on the *N*-methyl-D-aspartate (NMDA) receptor. We found previously that exogenously administered PA modulate the anxiolytic effects of some 1,4-benzodiazepines.[6] The present work was aimed at determining whether antidepressive activity of imipramine (IMI) is also affected by PA. Moreover, the MK-801, a noncompetitive NMDA receptor antagonist[7] was used because it was found to affect the IMI activity in rats.[8]

MATERIALS AND METHODS

The experiments were carried out on nonfasted male Wistar rats. IMI (10 mg/kg) was administered intraperitoneally twice: 24 and 1 h before the test; in a second experiment it was given nine times: once a day for nine days with the last dose given 1 h before the test. PUT (200 mg/kg), SPD (80 mg/kg), and SPM (40 mg/kg) were given 1 h prior to the test. MK-801 (0.1 mg/kg) was injected 30 min after the last dose of drugs. The antidepressant effect of IMI was assessed in the forced swimming test.

RESULTS

After a single injection of PA, only the PUT-treated group was immobile for a shorter time than control: 171.0 ± 13.6 s and 231.0 ± 6.0 s, respectively ($p < 0.05$ vs. control). PUT was as effective as IMI given twice: 157.8 ± 7.1 s ($p < 0.05$ vs. control). When PA were co-administered with IMI the reduced immobility was observed after injection of IMI + SPM: 106.7 ± 8.1 s ($p < 0.05$ vs. IMI-treated group). The combined treatment with SPD + IMI + MK-801 and SPM + IMI + MK-801

reduced significantly the immobility time: 92.5 ± 18.2 s and 97.0 ± 10.6 s ($p < 0.05$ vs. control and IMI-treated group), respectively.

In summary, these results suggest that different effects of PA on IMI activity could be mediated by an excitatory amino acid (EAA)-ergic system; however, for PUT + IMI, the GABA-ergic system must also be considered.

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